

(19) World Intellectual Property  
Organization  
International Bureau



(43) International Publication Date  
22 April 2004 (22.04.2004)

PCT

(10) International Publication Number  
WO 2004/033728 A2

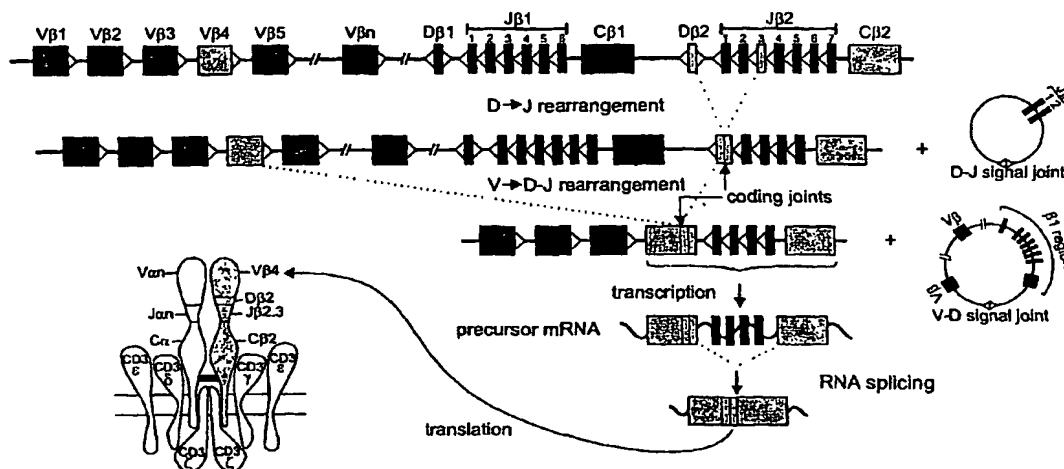
- (51) International Patent Classification<sup>7</sup>: C12Q 1/68
- (21) International Application Number:  
PCT/NL2003/000690
- (22) International Filing Date: 13 October 2003 (13.10.2003)
- (25) Filing Language: English
- (26) Publication Language: English
- (30) Priority Data:  
60/417,779 11 October 2002 (11.10.2002) US
- (71) Applicants (for all designated States except US): ERASMUS UNIVERSITEIT ROTTERDAM [NL/NL]; Dr. Molewaterplein 50, NL-3015 GE Rotterdam (NL). DAVI, Frederic, Bernard, Louls [FR/FR]; 7 Chemin de l'Ermitage, F-92130 Meudon (FR).
- (72) Inventors; and
- (75) Inventors/Applicants (for US only): VAN DONGEN, Jacobus, Johannes, Maria [NL/NL]; Parallelweg Zuid 147, NL-2914 LE Nieuwerkerk aan de IJssel (NL). LANGERAK, Anthonie, Willem [NL/NL]; van Bronkhorstvlies 34, NL-2992 WJ Barendrecht (NL). SCHUURING, Eduardus, Maria, Dominicus [NL/NL];

Eckhartstraat 54, NL-9746 BM Groningen (NL). SAN MIQUEL, Jesus, Fernando [ES/ES]; Calle Mizar 16, Urbanizacion Aldebaran, Santa Marta de Tormes, 37900 Salamanca (ES). GARZIA SANZ, Ramon [ES/ES]; Servicio de Hematologia, Avenida de Mirat 9 5-B, 37005 Salamanca (ES). PARREIRA, Antonio [PT/PT]; Rue Eca de Queros 17-1, 1050-095 Lissabon (PT). SMITH, John, Lewis [AU/GB]; Cobweb Cottage, North Common Lane, Landford, Wiltshire SP5 2EL (GB). LAVENDER, Frances, Louise [GB/GB]; White Copse, 16, Honey Lane, Burley, Ringwood, Hampshire BH24 4EN (GB). MORGAN, Gareth, John [GB/GB]; 18 Gledhow Wood Grove, Roundhay, Leeds, Yorkshire LS8 1NZ (GB). EVANS, Paul, Anthony, Stuart [GB/GB]; Pinfold Cottage, Caudle Hill, Fairburn, Yorkshire WF 11 9JR (GB). KNEBA, Michael [DE/DE]; Am See 4, 24259 Westensee (DE). HUMMEL, Michael [DE/DE]; Kaiserstrasse 4, 12105 Berlin (DE). MACINTYRE, Elizabeth, Anne [GB/FR]; 7 Chemin de l'Ermitage, F-92130 Meudon (FR). BAS-TARD, Christian [FR/FR]; 4 rue des Bouleaux, F-76680 Ardouval (FR).

- (74) Agent: PRINS, A.W.; Nieuwe Parklaan 97, NL-2587 BN Den Haag (NL).

[Continued on next page]

(54) Title: NUCLEIC ACID AMPLIFICATION PRIMERS FOR PCR-BASED CLONALITY STUDIES



(57) **Abstract:** The invention relates to PCR-based clonality studies for among others early diagnosis of lymphoproliferative disorders. Provided is a set of nucleic acid amplification primers comprising a forward primer, or a variant thereof, and a reverse primer, or a variant thereof, capable of amplifying a rearrangement selected from the group consisting of a VH-JH IGH rearrangement, a DH-JH IGH rearrangement, a VK-JK IGH rearrangement, a VK/intron-Kde IGH rearrangement, a Vλ-Jλ IGL rearrangement, a Vδ-Jδ TCRB rearrangement, a Dδ-Jδ TCRB rearrangement, a Vγ-Jγ TCRG rearrangement, a Vδ-Jδ TCRD rearrangement, a Dδ-Dδ TCRD rearrangement, a Vδ-Dδ TCRD rearrangement, or a translocation selected from t(11;14)(BCL1-IGH) and t(14;18)(BCL2-IGH). The primers can be used in PCR-based clonality studies for early diagnosis of lymphoproliferative disorders and detection of minimal residual disease (MRD). Also provided is a kit comprising at least one set of primers of the invention.



(81) **Designated States (national):** AE, AG, AL, AM, AT (utility model), AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ (utility model), CZ, DE (utility model), DE, DK (utility model), DK, DM, DZ, EC, EE (utility model), EE, EG, ES, FI (utility model), FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK (utility model), SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.

(84) **Designated States (regional):** ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW),

Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

**Published:**

— without international search report and to be republished upon receipt of that report

*For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.*